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Original Article

Short-term Vitamin D Supplementation for Non-Diabetic Elder Egyptians: Effects on Glycemic Indices and Lipid Profile

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ABSTRACT

Background and aim: Elderly populations are a susceptible group for many health risks. Vitamin D deficiency is a common health problem among elderly populations. It is associated with different harmful effects, especially increased insulin resistance and liability for development of diabetes mellitus. The value of vitamin D supplementation on glycemic indices produced heterogenous results. This work aimed to evaluate the value of vitamin D supplementation (10000 IU, three times a week for six months) on glycemic indices, mainly insulin resistance.

Methodology: This study included 100 apparently healthy elder subjects. They were randomly divided into two equal groups, the intervention and the control groups. The intervention group received vitamin D supplementation by 10000 IU three times a week for 6 months. However, the control (placebo) group, received a placebo at the same time for the same period. Laboratory values (vitamin D, fasting blood glucose and insulin, insulin resistance indicator (HOMA-IR) and lipid profiles) were measured at inclusion in the study and after 6 months of treatment. In addition, demographic characteristics were documented.

Results: At basal point, both intervention and control groups were comparable regarding patient demographics and all laboratory workup values. There was slight increase of males than females in both groups. The mean age was 68.32±3.93 and 69.60±3.75 years in intervention and control groups respectively. After the six months of vitamin D supplementation, the intervention group had significantly higher levels of vitamin D than the control group (28.48±3.58 vs 12.42±1.99 ng/ml, respectively). However, the values of fasting glucose, fasting insulin, HOMA-IR and total cholesterol were significantly reduced in the intervention than the control group. In the intervention group, all laboratory work-up values showed significant changes at the end of the study duration than basal values. For example, vitamin-D values were increased from 11.66±2.20 to 28.48±3.58 ng/ml.

Conclusion: Supplementation with cholecalciferol for 6 months is associated with improvement of vitamin D status, insulin resistance indicator (HOMA-IR), overall glycemic indices and lipid profile in healthy elder Egyptians.

Keywords: Cholecalciferol; Glucose; Insulin Resistance; Elderly.

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INTRODUCTION

Vitamin-D is an important vitamin concerned with the regulation of calcium metabolism, bone formation and resorption. In addition, vitamin D seems to have a role in the pathogenesis of diabetes mellitus (DM), both types 1 and 2. Previous studies reported an inverse correlation between serum levels of vitamin D and fasting blood glucose concentration. In addition, vitamin D deficiency is increased in patients with type-2 diabetes mellitus (T2DM) especially in elderly [(1-3)].

The hallmark pathogenetic aspect in diabetes is the insulin resistance (IR) (impaired sensitivity and/or secretion). Vitamin D-deficiency is also associated with IR and reduced insulin secretion due to beta-cell dysfunction [(4-7)]. However, the effects of supplementation by vitamin-D on glucose homeostasis are contradictory [(8-12)].

IR are reported to be increased with age and it is correlated with abdominal obesity and reduced serum levels of vitamin D as well [(13,14)].

This study aimed to assess the effect of Vitamin-D supplementation on insulin resistance and metabolic indicators in non-diabetic elderly with vitamin D deficiency.

SUBJECTS AND METHODS

This study included 100 ambulatory elderly subjects. They were non-diabetic and had vitamin-D deficiency (< 30 ng/ml) [(15)]. However, we excluded patients with T2DM, chronic medical disease (e.g., renal failure, hepatic ell failure, congestive heart failure, cancer or those on oral hypoglycemic drugs or statins. In addition, patients with bone diseases are excluded. All subjects were recruited from the outpatient clinics of Internal Medicine Departments, Al-Azhar University Hospitals (Cairo and Damietta).

The study protocol was explained for each patient and an informed consent was obtained. In addition, the study protocol was approved by the local research and ethics committee of Al-Azhar Faculty of Medicine (Damietta). The study was completed between January to December 2019.

Subjects were randomly (simple randomization by closed envelop method) classified into two equal groups. The first (intervention group) was the study group who received 10000 IU of vitamin D (cholecalciferol) three times a week for 6 months. The second was the control group, where subjects received placebo three times a week for 6 months. The placebo tablet was formed of cellulose (66.0%), starch (33.5%), and magnesium stearate (0.5%).

The laboratory workup was performed at the start of the study and after the end of the 6-months of supplementation. Subjects were checked on monthly intervals to check the compliance.

Laboratory workup included serum glucose levels, insulin, vitamin D (by radioimmunoassay) and glycated hemoglobin (HbA1c). An automated analyzer (ROCHE, Cobas 8000 (C701 & C702) was used for determination of different laboratory indicators. Other laboratory measurements included lipid profile measured by autoanalyzer (RA1000 autoanalyzer (Bayer Diagnostics, Suffolk, U.K.)

The primary outcome was the insulin resistance index (HOMA-IR). It was measured from the equation (HOMA-IR = [insulin (mU/L) x glucose (mmol/L)]/22.5. Values were compared between groups and between basal and last values in intervention group.

In addition, anthropometric measurements were determined (weight and height) to calculate body mass index (BMI) from the equation (weight (kg) divided by square of the body height in meters).

Data analysis: The collected data was anonymized by coding and fed to personal computer. The normally distributed continuous data was expressed by their arithmetic mean and standard deviation (SD). On the other side, relative frequency and percentages were used to summarize categorical variables. The two groups were compared by independent samples student "t" test at the baseline and after the 6 months. Values at the start and at the end in the same group were compared by paired samples "t" test. On the other side, categorical data were compared by Chi square test. The SPSS (Statistical package for social sciences) was used for statistical analysis. P value < 0.05 was considered significant.

RESULTS

One hundred subjects were included and divided equally into two groups, intervention and control groups (each 50 subjects). Both groups were comparable regarding patient demographics and basal values of fasting blood sugar, fasting insulin, glycated hemoglobin, insulin resistance index and lipid profile. There was slight increase of males than females in both groups. The mean age was 68.32±3.93 and 69.60±3.75 years in intervention and control groups respectively (details are presented in table 1).

After the six months of vitamin D supplementation, the intervention group had significantly higher levels of vitamin D than the control group (28.48±3.58 vs 12.42±1.99 ng/ml, respectively). However, the serum values of fasting glucose, fasting insulin, insulin resistance index and total cholesterol were significantly reduced in the intervention than the control group. However, the values of glycated hemoglobin, LDL cholesterol and HDL cholesterol, showed non-significant differences between the intervention and control groups (Table 2).

In the intervention group, all laboratory work-up values showed significant changes at the end of the study duration than basal values. For example, vitamin-D values were increased from 11.66±2.20 to 28.48±3.58 ng/ml. Fasting blood sugar, fasting insulin, glycated hemoglobin, insulin resistance indicator (HOMA-IR), total cholesterol and LDL cholesterol were significantly reduced at the end than basal values. However, there was no significant change for HDL cholesterol (Table 3).

Interestingly, in the control group, there was significant changes in vitamin D levels, Fasting insulin, Insulin resistance, total cholesterol and LDL cholesterol (Table 4).

Table (1): Patient demographics and basal values of glucose indicators, vitamin D and lipid profile

Variable		Intervention	Control group	Test	P
Sex (n, %)	Male	28 (56)	30 (60)	0.16	0.42
	Female	22 (54)	20(40)		
Age (year)	Mean±SD	68.32±3.93	69.60±3.75	0.364	0.716
BMI (kg/m²)	Mean±SD	26.11±2.01	25.58±1.57	1.43	0.155
Smoking (n, %)		18(36)	20(40)	0.17	0.68
Vitamin-D (ng/ml)	Mean±SD	11.66±2.20	12.22±2.13	1.29	0.199
FBG (mmol/L)	Mean±SD	4.48±0.31	4.44±0.24	0.712	0.478
FBI (mU/L)	Mean±SD	12.76±1.55	12.78±1.40	0.054	0.957
HbA1c (%)	Mean±SD	5.41±0.26	5.32±0.34	1.52	0.131
HOMA-IR	Mean±SD	2.54±0.30	2.52±0.32	0.189	0.850
Total cholesterol (mmol/L)	Mean±SD	1.39±0.39	1.53±0.46	1.63	0.105
LDL cholesterol (mmol/L)	Mean±SD	1.20±0.14	1.15±0.13	1.75	0.083
HDL cholesterol (mmol/L)	Mean±SD	0.92±0.18	0.89±0.15	1.15	0.251

BMI: body mass index; FBG: fasting blood glucose, FBI: fasting blood insulin, LDL: low density lipoprotein, HDL: High density lipoprotein.

Table (2): Laboratory values at the end of study duration

Variable	Intervention	Control group	Test	P
Vitamin-D (ng/ml)	28.48±3.58	12.42±1.99	27.70	*<0.001**
FBG (mmol/L)	4.25±0.28	4.40±0.22	2.96	*0.004**
FBI (mU/L)	11.60±1.30	12.73±1.39	4.18	*<0.001**
HbA1c (%)	5.39±0.27	5.32±0.34	1.01	0.319
HOMA-IR	2.19±0.26	2.50±0.32	5.24	*<0.001**
Total cholesterol (mmol/L)	1.29±0.36	1.51±0.45	2.75	*0.007**
LDL cholesterol (mmol/L)	0.916±0.15	0.880±0.14	1.19	0.237
HDL cholesterol (mmol/L)	1.12±0.12	1.11±0.10	0.234	0.815

FBG: fasting blood glucose, FBI: fasting blood insulin, LDL: low density lipoprotein, HDL: High density lipoprotein

Table (3): Paired comparison in intervention group

Variable	Before	After	Paired "t"	P value
Vitamin-D (ng/ml)	11.66±2.20	28.48±3.58	*32.27*	*<0.001**
FBG (mmol/L)	4.48±0.31	4.25±0.28	*13.55*	*<0.001**
FBI (mU/L)	12.76±1.55	11.60±1.30	*8.92*	*<0.001**
HbA1c (%)	5.41±0.26	5.39±0.27	*2.605*	*0.012**
HOMA-IR	2.54±0.30	2.19±0.26	*12.22*	*<0.001**
Total cholesterol (mmol/L)	1.39±0.39	1.29±0.36	*7.25*	*<0.001**
LDL cholesterol (mmol/L)	1.20±0.14	0.916±0.15	*8.253*	*<0.001**
HDL cholesterol (mmol/L)	0.92±0.18	1.12±0.12	1.273	0.209

FBG: fasting blood glucose, FBI: fasting blood insulin, LDL: low density lipoprotein, HDL: High density lipoprotein.

Table (4): Paired comparison in control group

Variable	Before	After	Paired "t"	P value
Vitamin-D (ng/ml)	12.22±2.13	12.42±1.99	4.07	<0.001*
FBG (mmol/L)	4.44±0.24	4.40±0.22	1.79	0.079
FBI (mU/L)	12.78±1.40	12.73±1.39	*4.95*	*<0.001**
HbA1c (%)	5.32±0.34	5.32±0.34	0.33	0.74
HOMA-IR	2.52±0.32	2.50±0.32	*2.51*	*0.015**
Total cholesterol (mmol/L)	1.53±0.46	1.51±0.45	*3.93*	*<0.001**
LDL cholesterol (mmol/L)	1.15±0.13	0.880±0.14	*5.39*	*<0.001**
HDL cholesterol (mmol/L)	0.89±0.15	1.11±0.10	1.00	0.322

FBG: fasting blood glucose, FBI: fasting blood insulin, LDL: low density lipoprotein, HDL: High density lipoprotein.

DISCUSSION

The use of vitamin-D supplementation (10,000 IU vitamin-D three times a week) for six months in older non-diabetic subjects was associated with improvement in glycemic indices and lipid profile.

These results are comparable to those reported by **El Hajj *et al.*** [16] who reported that, three times weekly oral supplementation by 10,000 IU cholecalciferol for 6 months in healthy older adults resulted in improvement of fasting blood glucose (FBG), HOMA-IR, as well as LDL cholesterol. The results of the current study confirm previous studies reported a beneficial effects of vitamin D on insulin resistance and metabolic syndrome.

For example, **Baynes *et al.*** [17] reported a significant and inverse correlation between fasting insulin and values of serum vitamin-D in 134 healthy older subjects. This correlation was confirmed independent of the body mass index, smoking habits, alcohol consumption and the levels of physical activity.

In addition, **Hurskainen *et al.*** [18] reported that, serum values of vitamin D were inversely associated with fasting insulin, fasting glucose and oral glucose tolerance tests after adjustment for gender and age. They concluded that, low levels of serum vitamin D are associated with impaired glucose and insulin metabolism

Results are also consistent with **Mousa *et al.*** [19] who reported comparable results and suggested that, the association between vitamin D and glycemic indices in healthy adults are mediated through adiposity.

Von Hurst *et al.* [20] reported that supplementation with vitamin D was associated with improvement of insulin sensitivity and IR, and reduction of fasting insulin when compared to placebo.

Chiu *et al.* [21] also reported a significant correlation between vitamin D levels and insulin sensitivity

On the other side, **Tai K, *et al.*** [22] reported that, in non-diabetic adults, the correction of vitamin-D deficiency was no associated with any significant effects on the glycemic indices (glucose and insulin concentrations, insulin sensitivity) irrespective of positive association detected with oral glucose tolerance tests. They concluded that, their observation did not support the association between glycemic indices and vitamin D at least at short-term. However, they used vitamin Supplementation for two days per week for only two weeks.

In addition, the difference in the characteristics of included subjects, the study duration and use of lower doses of vitamin D could explain the contradictory results.

The mechanisms by which vitamin D exerts its beneficial effects on glycemic indices is heterogenous and it was reported that, with vitamin D deficiency, there is a reduction in the function of the pancreatic beta-cell, which reestablished with correction of vitamin D by supplementation [23]. Another supported hypothesis is the improvement of insulin resistance by vitamin D supplementation and reduction of diabetes risk in healthy adults. This achieved by regulation of insulin action and release [24].

The reduction in total cholesterol and LDL cholesterol at the end of the study is remarkable and consistent with earlier studies reported that, vitamin D or a calcium vitamin D combination could be beneficial on reduction of cholesterol concentrations in pre- and postmenopausal women [25].

Conclusion: vitamin D supplementation is associated with improvement of glycemic indices mainly insulin resistance and lipid profile in healthy elderly Egyptian subjects.

The double blind and controlled nature of the study is one of strengthens of this study, especially with higher prevalence of vitamin D deficiency among the studied age group (elderly). In addition, the dose of vitamin D was adequate to reveal changes in the study outcomes. However, the small sample, short duration of the study and the use of only HOMA-IR as the main outcome are limitations of the current work.

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